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Note

A facile synthesis of *tert*-butyl and other alkyl β-D-gluco- and -galacto-pyranosides

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The yields of *tert*-butyl glycosides reported in the literature[1–5] are moderate, and purification can be laborious due to the formation of side products (*e g*, 1,2-orthoesters) *tert*-Butyl glycosides are useful, as the inductive effect of the *tert*-butyl group activates the glycosidic oxygen, and this effect has been applied in an improved synthesis of β,β-trehalose octa-acetate[6]

The enhancement[7] of the Koenigs–Knorr reaction between 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide and methanol by a factor 10^3–10^4 in the presence of silver salicylate prompted an investigation of the behaviour of other simple alcohols, including *tert*-butyl alcohol The use of this salt in glycosylations of complex alcohols has been reported[8]

The reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and -galacto-pyranosyl bromide with alcohols in the presence of silver salicylate was very rapid, even for the more sterically hindered alcohols The rate of this heterogeneous reaction could

TABLE I

DATA FOR SOME ALKYL 2,3,4,6-TETRA-*O*-ACETYL-β-D-GLYCOPYRANOSIDES

Alkyl group	*Parent sugar*	*Reaction time (min)*[a]	*Yield (%)*	*M p (degrees)*	$[\alpha]_D$ (c 2, *chloroform*) *(degrees)*
Methyl[3]	D-Glucose	5	97	103–104	−18
Ethyl[3]		10	95	106–107	−23
1-Propyl[3]		15	81	102–103	−21
2-Propyl[3]		15	86	137–138	−23
1-Butyl[3]		30	78	65–66	−21
tert-Butyl[5]		30	75	143–144	−13
Methyl[7]	D-Galactose	5	93	95–96	−14
Ethyl[14]		10	90	86–87	−15
2-Propyl[c]		15	80	58–59	−15
tert-Butyl		30	56[b]	—	—

[a]Refers to duration of stirring (see Experimental) [b]Yield of deacetylated, freeze-dried product [c]Found C, 52 24, H, 6 67 $C_{17}H_{26}O_{10}$ calc C, 52 30, H, 6 71

not be determined, because it is likely to be dependent on the crystal size of the silver salicylate and on the solubility of the glycosyl bromide The yields of products are given in Table I

The reaction with methanol gave the β-glycoside only but, with 2-propanol and *tert*-butyl alcohol, substantial proportions of the respective 1,2-orthoesters were also formed, as shown by t l c and ^{1}H-n m r spectroscopy Where the presence of 1,2-orthoesters complicated the recrystallization of glycosides, recrystallization was effected from acidified, aqueous acetone, in which the 1,2-orthoesters were hydrolysed

Crude *tert*-butyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside contained small amounts of 2,3,4,6-tetra-*O*-acetyl-1-*O*-salicyloyl-D-glucopyranose[9], as, after treatment with methanolic sodium methoxide, the odour of methyl salicylate was detected 2,3,4,6-Tetra-*O*-acetyl-1-*O*-salicyloyl-β-D-glucopyranose becomes the main product if the reaction is carried out in weakly nucleophilic alcohols (*e g* , allyl alcohol or 2,2,2-trichloroethanol) or in alcohols which dissolve silver salicylate (*e g* , 2-methylthioethanol[10]) On the other hand, the use of an additional solvent increases the relative yields of the respective 1,2-orthoesters[8 10]

The yields of glycosides from primary, secondary, and tertiary alcohols were good (Table I) and the method, which is suitable for large-scale preparations (up to 200 g), is rapid and economic, the alcohols and silver salts may be recovered in good yields

The acid-catalysed hydrolysis of *tert*-butyl glycosides mainly involves bond fission between the *tert*-butyl group and the glycosidic oxygen atom[5 11 12] Hydrolysis of *tert*-butyl β-D-glucopyranoside was complete within 3 min in trifluoroacetic acid (cellobiose and 2-propyl β-D-glucopyranoside were stable for up to 15 min under similar conditions), and within 5 min in dichloromethane–trifluoroacetic acid (1 2)

EXPERIMENTAL

General methods — Melting points are corrected, Solutions were concentrated at 40° (bath)/~14 mmHg Specific rotations were determined at 22° with a Perkin–Elmer 141 polarimeter ^{1}H-N m r spectra were recorded with a Varian EM360 spectrometer for solutions in $CDCl_3$ (internal Me_4Si) T l c was performed on silica gel (Schleicher & Schull T L C Plastic Foil FR-1500) with conventional detection by charring with sulphuric acid The following solvents were used for t l c and column chromatography (silicic acid) *A*, chloroform–methanol (25 1), *B*, acetic acid–ethyl acetate–water–1-butanol (6 3 1 8), *C*, ethyl acetate–2-propanol–water (5 5 2)

Alkyl 2,3,4,6-tetra-O-acetyl-β-D-gluco- and galactopyranosides — A mixture of silver salicylate[8 9] (9 g, 37 mmol) and a suspension or solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromide (10 g, 24 mmol) in the appropriate alcohol (300 ml) was stirred for 5–30 min (Table I) to obtain a precipitate of silver bromide that is convenient to filter over diatomaceous earth, small amounts of silver bromide in the filtrate may seriously affect the yields of the *tert*-butyl glycoside The filtrate

was concentrated under reduced pressure, and *tert*-butyl alcohol was removed at atmospheric pressure The residue was added to a chloroform extract (5 × 40 ml) of the insoluble silver salts, and the solution was washed with an ice-cold, aqueous solution (120 ml) of potassium cyanide (0 5 g) and potassium carbonate (10 g), and then water, dried (Na_2SO_4), and concentrated The methyl, ethyl, 1-propyl, and 1-butyl glycosides (Table I) were crystallized from ether–hexane T l c (solvent *A*) of the crude products revealed 1,2-orthoesters [δ 1 77 (*exo* Me-2) and 1 68 (*endo* Me-2)] and traces of 2,3,4,6-tetra-*O*-acetyl-D-glycoses as contaminants To destroy the othoesters in the crude 2-propyl and *tert*-butyl glycosides, the crude product was dissolved in acetone (40 ml) and M hydrochloric acid (20 ml), and water (15 ml) was added dropwise. The product was collected at 0°, washed with ice-cold acetone–water (6 5), and dried over potassium hydroxide *in vacuo* The 2-propyl glycosides were crystallized from ether–hexane, and *tert*-butyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside from ethanol

tert-Butyl β-D-galactopyranoside tetra-acetate failed to crystallize When purified by deacetylation (Zemplén), followed by column chromatography (solvent *C*) to remove D-galactose and reacetylation, the syrupy product had $[\alpha]_D$ +1° (*c* 3 3, chloroform) (Found C, 53 17, H 6 87 $C_{18}H_{20}O_{10}$ calc C, 53 46, H, 6 98)

The n m r spectrum of the product was identical to that previously reported[12]

Hydrolysis of the tert*-butyl glycosides* — Samples (10 mg) of *tert*-butyl D-glucopyranoside (obtained by deacetylation[11] of the tetra-acetate) or D-galactopyranoside were dissolved in trifluoroacetic acid (1 ml) Removal of the *tert*-butyl group was complete within 3 min (t l c , solvent *B*) Cellobiose and 2-propyl β-D-glucopyranoside were stable for up to 15 min, but sucrose was hydrolysed[11] *tert*-Butyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (500 mg, 2 24 mmol) was dissolved in dichloromethane (5 ml), and trifluoroacetic acid (10 ml) was added The *tert*-butyl group was quantitatively removed within 5 min (t l c , solvent *A*), sucrose octa-acetate was stable for up to 15 min under these conditions The solution was concentrated to give 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (222 mg, 52%), m p 119–120° (from ether–hexane), $[\alpha]_D$ +30 → +74° (*c* 2, ethanol), lit [13] m p 120–122°, $[\alpha]_D$ +33 → +79° (*c* 1 9, ethanol)

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